IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

UNITED STATES OF AMERICA	:	CRIMINAL ACTION
	:	
v.	:	
	:	NO. 09-403-3
MICHAEL D. HUGGINS	:	

MEMORANDUM

Legrome D. Davis, J. December 13, 2011

On November 21, 2011, a nine-month sentence of imprisonment was imposed on Defendant Michael D. Huggins, who pled guilty as a responsible corporate officer for violations of the Food Drug and Cosmetic Act (FDCA), 21 U.S.C. §§ 301-399d; see 21 U.S.C. §§ 351(f)(1)(B), 352(f) and (o), 331(a), 333(a)(1). The sentence varied upward from the applicable Sentencing Guidelines range of 0 to 6 months for imprisonment. The variance is warranted because a Guidelines sentence would not adequately address the unprecedented nature of the criminal conduct of Huggins and his co-Defendants. The scope of their scheme is without parallel, the risks created for an unsuspecting public were grave, and the scale of the deception of the Food and Drug Administration can only be characterized as extreme.

At sentencing, Defendant orally moved pursuant to 18 U.S.C. 3143(b)(1)(B)(iv)[1] for

[1] The statute, 18 U.S.C. § 3143(b)(1)(A), (B)(iii), and (B)(iv), provides in pertinent part:

> [A] person who has been found guilty of an offense and sentenced to a term of imprisonment, and who has filed an appeal . . . , [shall] be detained, unless the judicial officer finds –
>
> (A) by clear and convincing evidence that the person is not likely to flee or pose a danger to the safety of any other person or the community if released . . . ; and
>
> (B) that the appeal is not for the purpose of delay and raises a substantial question of law or fact likely to result in – . . .
> (iii) a sentence that does not include a term of imprisonment, or
> (iv) a reduced sentence of imprisonment less than the total of the time already served plus the expected duration of the appeal process. . . .

release at the expiration of six months, absent a contrary ruling by a court. Transcript of Sentencing of Michael D. Huggins ("Sentencing Tr."), 83:2-86:3, Nov. 21, 2011. The motion for release was denied and Defendant was remanded to custody. On December 2, 2011, Defendant filed a notice of appeal of the final judgment entered on November 22, 2011 and the denial of the motion for release. (Doc. No. 178)

Medical devices are subject to the regulation and control of the Food and Drug Administration (FDA). The FDA's regulation centers on the degree of regulatory control necessary to ensure the safety and efficacy of a particular medical device. Class III significant risk devices are the most intensely regulated devices because the devices present a potential, serious risk of illness or injury. See 21 U.S.C. §§ 351, 360c, 360e, 360j; ; 21 C.F.R. § 812.3(m) (A "significant risk device" is one that presents a potential for serious risk to the health, safety, or welfare of a subject."). The regulations are of substantial importance in preventing impairment of human health. Typically, since minimal safety information as to these devices exists prior to FDA approval, Class III devices gain approval only after successful completion of the FDA's most stringent review process – a lengthy undertaking that includes a careful examination of valid scientific test data. Only in this way can the FDA satisfy its duty to the public to ensure the safety and effectiveness of significant risk devices. Class III devices typically require premarket approval (PMA) or an investigational device exemption (IDE). The Synthes products at the heart of this case are Class III devices.

The 510(k) route is an alternate method for securing approval for medical devices, including Class III devices, where the manufacturer demonstrates that the new device is at least as safe and effective as a previously approved, or predicate, device. A 510(k) approval requires a showing of "substantial equivalence" to the predicate device. This means the new device will be used for the same purposes as the previously approved device, and the proposed device does not raise new questions of safety and effectiveness. This is a less intense, and much briefer, review process.

Defendant Huggins was hired by Synthes at the end of 1994. From 1999 through January 2004, he served as President of Synthes North America, Inc., a subsidiary of Synthes, Inc. From February 2004 through January 7, 2007, he held the position of President of Global Synthes Spine Division. Presidents of the company's other units, such as Defendant Thomas B. Higgins, President of the Spine Division, reported directly to Huggins. Huggins was the most senior, responsible officer on the line of command before the Chief Executive Officer of Synthes' multinational business enterprise, Hansjörg Wyss. Huggins reported directly to Wyss.

Huggins pled guilty as a responsible corporate officer to the introduction into interstate commerce of adulterated and misbranded medical devices – in this case, two Class III significant risk medical devices, SRS mixed with barium sulphate and XR – in violation of 21 U.S.C. §§ 331(a) and 331(a)(1). Plea Agreement, ¶¶ 1, 9(a)-(j). These devices were adulterated because they were required to have, but did not have in effect an approved application for premarket approval or an approved investigational device exemption. Id. § 351(f)(1)(B). In part, the devices were misbranded because their labeling did not bear "adequate directions for use," id. § 352(f), and because the FDA was not provided with timely premarket notification of a new intended use prior to the introduction of the devices into interstate commerce for such use, id. § 352(o). The maximum statutory penalty for any person who violates a provision of § 331 is imprisonment for not more than one year. Id. § 333(a).

Although both devices were eventually cleared for use in the spine as general bone void fillers, neither device was ever cleared for use in load-bearing applications or for use in procedures to treat vertebral compression fractures, such as vertebroplasty[2] and kyphoplasty.[3]

FACTUAL FINDINGS[4]

1. In July 1999, Synthes acquired Norian Corporation, a manufacturer and seller of two calcium phosphate bone cements, Norian Cranial Repair System ("CRS") and Norian Skeletal Repair System ("SRS"). SRS had been approved by the FDA to be marketed for use in the distal radius, a long bone in the arm. Upon acquisition of Norian, Synthes began exploring new uses for the bone cements. In February 2000, Hansjörg Wyss, announced to Synthes personnel "a strong push for vertebroplasty". See G. Ex. 2, Government's March 26, 2010 Presentence Memorandum (G Ex. 1 through G Ex. 81), Doc. Nos. 93 and 94.

   In early 2000, Synthes planned to conduct a clinical trial of SRS without the FDA's approval. This was reflected in Thomas B. Higgins' February 24, 2000 e-mail to CEO Hansjörg Wyss, captioned "SRS for Spinal Applications – Action Plan Proposal." G. Ex. 3. The plan amounted to a clinical trial before SRS was cleared for use as a general bone void filler in the spine. The plan was to identify surgeons, select test sites, provide SRS product, train surgeons, observe surgeries, and compile and review data. 510(k) clearance for SRS was obtained on December 20, 2001.

2. A number of Synthes' regulatory personnel strenuously warned in 2000 and 2001 that a clinical trial of SRS would be illegal. See, e.g., June 21, 2007 Report of Interview of Barry E. Sands, former Synthes Group Manager, Regulatory and Clinical Spine during 2000-2003 ("Sands Interview"), submitted at the evidentiary hearing held in this case on June 6-7, 2011, as Huggins' Hr'g Ex. 6 at 2, 3, 5; March 19, 2001 e-mail from Michael

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[2] Merriam Webster's Medical Dictionary defines "vertebroplasty" as "a medical procedure for reducing pain by a vertebral compression fracture (as that associated with osteoporosis) that involves injection of an acrylic cement (as methyl methacrylate) into the body of the fractured vertebra for stabilization – compare KYPHOPLASTY."

[3] Merriam Webster's Medical Dictionary defines "kyphoplasty" as "a medical procedure that is similar to vertebroplasty in the use of acrylic cement to stabilize and reduce pain associated with vertebral compression fracture but that additionally restores vertebral height and lessens spinal deformity by injecting the cement into a cavity created in the fractured bone by the insertion and inflation of a special balloon."

[4] These facts are principally derived from exhibits to the government's March 26, 2010 Presentence Memorandum, Doc. Nos. 93 and 94, which will be referred to as "G Ex. __ ." Our focus is on Huggins' own conduct, the actions of his subordinates which Huggins ratified, and external events which were contemporaneously brought to Huggins' attention.

Sharp/Synthes Regulatory to co-Defendant Richard E. Bohner, Vice President of Operations who reported directly to Defendant Huggins until February 2004, captioned, "Spine [T]est Market for SRS," G Ex. 18.

Huggins received at least one warning through an August 23, 2000 e-mail from Michael Sharp, which Bohner forwarded to Huggins, G Ex. 17; see also G Ex. 18. Sharp warned against promoting off-label use of SRS without clearance from the FDA, stating in part:

> "As everyone is well aware, I hope, we do not have a spine indication for Norian SRS at this time. . . . We cannot promote the use of SRS for unapproved indications, and this is especially true for use in the spine, where FDA has previously made it clear to Norian that any intra-spinal use would require additional approval. . . . We are aware that the spine PD group has been considering developing a delivery system which could be used for vertebroplasty with any substance . . . . However, any suggestion on our part that the instrument could be used with SRS would be considered promotion of an unapproved use of SRS."

3. Two of Dr. Delamarter's patients suffered hypotensive, and nonfatal, events[5] on February 8, 2001 during vertebroplasty/kyphoplasty procedures using CRS, a precursor Norian device that had the same calcium phosphate formulation as SRS. At that time, CRS was not cleared by the FDA for use in the spine. In March 2001, Huggins learned about the Delamarter hypotensive events. See January 28, 2003 e-mail from Bohner to Higgins, attaching Huggins' March 29, 2001 e-mail, G Ex. 52. Huggins knew that a Synthes sales representative had been present at the off-label Delamarter surgeries.

   Huggins addressed this off-label, and therefore illegal, promotion in his March 16, 2001 e-mail, captioned, "Dr. R. Delamarter. He wrote: "You need to real [reel] the salesforce in ASAP." G Ex. 26.

4. Huggins attended the November 15, 2001 Synthes – Stratec Spine Management Review Board Meeting. CEO Hansjörg Wyss and Higgins also participated. Minutes at 1, 2-3, G Ex. 5. At the meeting, "Tom Higgins asked if we should consider a long-term IDE clinical study to follow-up patients with the vertebroplasty technique." Id. A decision was made not to pursue an IDE clinical study for SRS mixed with barium sulphate and instead, "to get a few sites to perform 60-80 procedures and help them publish their clinical results." Id.

   The safer and lawful approval route was expressly rejected. Huggins' single reported comment evinces an understanding of the correct route for examination of the

[5]The Delamarter case studies revealed "3-5 minutes following injection the patient[s] experienced a severe drop in blood pressure"), G Ex. 37 at 1DOJSYN.089.000325-.000351

vertebroplasty technique.

The Addendum to the MRB Meeting Minutes reveals that Wyss, Huggins, and Higgins later met and discussed Dr. Sohail Mizra's [University of Washington] presentation at the annual meeting on vertebroplasty and the serious nature of complications associated with the procedure. They ratified the decision to proceed via a limited test market involving at least 50 patients, whose cases would be followed before the Synthes product would be released to the broad medical market. Addendum, G Ex. 5 at 3.

At the time this decision was made, Huggins along with Synthes' other most senior executives knew that an IDE was required but it would be costly. An IDE would take about three years and a million dollars, and it was also clear that whatever competitive advantage Synthes continued to enjoy in the bone cement market would be lost. It was also known that Synthes' planned clinical trials on humans could not be lawfully conducted. See Sands Interview at 2, Huggins Hr'g Ex. 6.

5. On December 20, 2001, the FDA gave a 510(k) clearance for use of SRS as a general bone void filler in the spine, but only for "bony voids or defects that are not intrinsic to the stability of the bony structure." The label warned: "Do not mix . . . with any other substance." G Ex. 11.

6. During a May 8, 2002 telephone conference with Barry Sands and other Synthes personnel, the FDA noted the confusion that the current labeling procedures might cause over whether the bone fillers could be used in load-bearing areas. In particular, the "FDA expressed concern over the imprecision of the spine indication in the current indications for use of bone void fillers. . . . FDA asked that we provide additional labeling that specified load bearing indications, such as vertebroplasty, are not included in the current indication for use." Minutes, G Ex. 13. Sands stated that Synthes would "not promote this material (Norian XR) for such indications as vertebroplasty or other load bearing applications without the appropriate regulatory clearance." Id.; Sands Interview, Huggins' Hr'g Ex. 6 at 3, 3-4. Barry Sands recalled that the FDA was insistent on language warning about use in load-bearing applications and vertebroplasty. Sands Interview, Huggins' Hr'g Ex. 6 at 3-4. "Sands indicated that Synthes, including upper level management, clearly understood that Norian XR was not to be used for vertebral compression fracture procedures because the vertebral body '. . . is load bearing.' Sands stated there is no way it could [be claimed] he never made them aware of this." Id. at 4.

Defendant Huggins was fully informed about the call and the FDA's concerns and requirements. Agenda and minutes for September 17, 2002 Synthes – Stratec Spine MRB Meeting, G Exs. 35, 36 at 1DOJSYN.073.001959. Also, the minutes of the FDA call were attached to Synthes' subsequent Special 510(k) submission for clearance of XR as a general bone void filler, which was granted on December 19, 2002. G Exs. 13, 43, 44. The label cleared for XR included a warning bullet: "Not intended for treatment of vertebral compression fractures." G Ex. 46.

7. In April 2002, the University of Washington began pilot studies on SRS commissioned by Synthes. One researcher, Dr. Jens Chapman, in a May 4-6, 2002 e-mail to Nisra Thongpreda/original Synthes Group Product Manager for SRS-S (which became XR) explained the alarming effect of SRS on a pig:

> "[T]he entire pulmonary artery system had clotted off. This could represent an uncontrolled activation of the coagulation cascade. . . . This clearly underscores the need for further investigation of the device while it is in the 'medication phase' . . . .
> [W]e were expecting to kill the pig . . . but not suddenly and with a relatively small dose. We also need to worry about a coagulogenic effect of the substance itself. . . ."

Higgins received this e-mail. G Hr'g Ex. 3, submitted at the evidentiary hearing in this case on June 6-7, 2011. Thus, no later than May 2002, see G Ex. 8, Huggins knew that the chemical composition of SRS – the specific formula of the calcium phosphate cement – itself posed lethal risks when used in the spine in vertebroplasties. He knew the cement was potentially dangerous in that it appeared to have a rapid and extreme coagulogenic effect in the blood of animals. He knew, or should have known, that the planned development of a cement to treat vertebral compression fractures was potentially suspect, and caution and strict adherence to regulatory procedure was required. Importantly, Huggins knew, or should have known, of the need for further testing before the product could be safely used on humans.

See also G Ex. 37 at 1DOJSYN.089.000366-.000395 (University of Washington studies and grant proposal presented to Huggins in July 2003).

8. Huggins sent a May 30, 2002 e-mail to Higgins, Bohner, and others at Synthes, expressing his "second thoughts" about the unauthorized clinical trial of SRS in vertebroplasties. G Ex. 8. Huggins wrote:

> "There appears to be some shipments being made of Norian for Spine use which we need to discuss. We discussed the need to perform a real study to test Norian. We shouldn't be sending out product without proper protocols, surgeons sponsors, etc. As you know, we have gone to great lengths in SUSA to train surgeons on Norian's use. It seems Spine is bypassing the needed blocking and tackling without thinking this all the way through.
>
> In addition, I had a long phone conversation with Dr. Lambert who is very concerned about the Spine plan. I am now having second thoughts. . . ."

9. On June 10, 2002, Dr. Kenneth Lambert, a Synthes medical consultant, strenuously warned Higgins and Thongpreda that unauthorized clinical trials of SRS with cavity creation instruments were being conducted and that the trials amounted to "human experimentation." G Ex. 32.

In that e-mail, which addressed Lambert's meeting with Thongpreda in the week prior, Dr. Lambert wrote:

> "You have presumably been given the green light to begin a controlled study on using SRS with vertebroplasty using the new cavitation instruments. . . . [G]iving SRS directly to a surgeon for him to use without any protocol (control), is not a controlled study . . . **[T]his action amounts to human experimentation whose only defense seems to be that it will be a small study. If there are many spine surgeons who, in spite of knowledge of foregoing, are comfortable using SRS, then you should be uncomfortable with those surgeons.**" (emphasis supplied) G Ex. 32.

Almost immediately, Huggins received a copy of this e-mail.

10. Out of concern that Huggins and CEO Hansjörg Wyss were not aware of the conduct of their subordinates, Dr. Lambert wrote to them separately. G Ex. 32. On June 11, 2002, Dr. Lambert warned:

> "We may not ever know exactly what was the mission with Nisra [Thongpreda] and company, but I think it is clear that the toothpaste almost got out of the tube while many important people were not in the loop . . . . SRS is different than any other of your products in that it is manufactured by the surgeon in the patient[']s body. This is how it is so different than a Titanium plate [a common Synthes product] . . . .
>
> The numbers of vertebroplasty are huge but not very surprising, and all the more reason to have already done the studies. SRS can contribute to Spine's numbers but I am concerned that the company could suffer serious consequences if this is not done properly. **Having the FDA take approval away may not be the worst consequence.** (emphasis supplied)
>
> I am attaching my response to a meeting held with Nisra and some other members of Spine last week which lays out my thoughts on this; for what they are worth from someone with a large experience and extensive reading on the subject of SRS. This is all so that you can be as informed as possible when you must take on these important decisions."

11. Huggins, along with CEO Hansjörg Wyss, Higgins, and Bohner, participated in a

September 17, 2002, Management Review Board Meeting. Vertebroplasty was prominent on the agenda. "Wyss inquired about the test market set up and how surgeons, who are interested in the product are to be trained." Agenda and minutes, G. Ex. 35. The meeting included a presentation on the "May 2002 – FDA conference call discussing XR submission requirements." G Ex. 36 at 1DOJSYN.073.001959. This was the conference call in which the FDA insisted that the product bear the warning that it was not to be used in vertebroplasties. At that time, Synthes assured the FDA that it did not intend to promote the product in such surgeries.

In regard to the topic of vertebroplasty, the minutes of September 17, 2002 meeting state:

> "The XR formulation will be mixed with the new Norian rotary mixer only. Launch requires on time testing and development of the rotary mixer."
> "Action Items: Product Development to continue with next generation system components."

G Ex. 35 at 3. Huggins participated in that decision to proceed with and fully launch the illegal XR test markets by December 2002.

12. On January 13, 2003, a patient of Dr. Barton Sachs, Texas Back Institute, Plano, TX died during a vertebroplasty/kyphoplasty using SRS mixed with barium sulphate. G Exs. 49, 50, 51. No medical device report (MDR) was filed and no autopsy was done.

13. Huggins learned of the January 13, 2003 death at some point in January 2003. Sentencing Tr. 19:24-20:8; see January 28, 2003 e-mail from Bohner to Higgins, attaching Huggins' March 29, 2001 e-mail, G Ex. 52.

    See also G Ex. 37 at 1DOJSYN.089.000325 (case study on death of Dr. Sach's patient presented to Huggins in July 2003: "~15 seconds after fill, blood pressure dropped and carbon dioxide levels rose"); G 38 at 1DOJSYN.089.000717 (PowerPoint presented to Huggins in July 2003, describing effect of SRS on Dr. Sach's patient: "immediately after injection, patient became hypotensive and CO2 levels rose").

14. On February 10, 2003, Huggins approved and signed the Final Market Introduction Plan for XR. G. Ex. R-3, United States' Consolidated Response to Defendants' Objections to Presentence Reports (G Exs. R-1 through R-33). The plan predicted a $3,211,031.53 first-year after-tax profit on an initial investment of $92,804.80, meaning an after-tax profit of 35 times the cost of raw materials. See Sentencing Tr. 27:19-29:23, 28:22-29:1

15. Huggins, along with Higgins and Bohner, participated in a July 18, 2003 Safety Meeting. See Packet of materials distributed to all attendees, G Ex. 37; PowerPoint, G Ex. 38; Minutes of meeting attended by Huggins, Higgins, and Bohner, G Ex. 39. Huggins was fully informed about the topics and participated in the discussions at this meeting about

the risks involved in the XR "release to market strategy." The packet of materials distributed to all attendees, G Ex. 37, stated in part:

> "Norian SRS with Barium Sulphate – Back Table Mixing. This part of the test market began in September 2002. [The FDA had not granted approval for the mixing process at that time.] Two sites were selected to participate. . . . Rollout of XR with Rotary Mixer. This expanded test market to begin in August 2003 includes eight test sites selected by Product Development plus eight test sites selected by AVPs [area vice presidents] and Regional Managers. The PD [product development] sites were selected based on publication interest, affiliation with treating vertebral compression fractures . . . . The last phase of the test market will occur in September 2003 . . . . These eight sties encompass the last of those chosen by AVPs and RMs [regional managers] . . . ."

Huggins along with the other participants explicitly evaluated whether to abandon the project, or pursue business interests over the safety of the patients. PowerPoint, G Ex. 38 ("release to market strategy" re: "Norian XR Options," including "Cancel project – Too unsafe."); Minutes, G Ex. 39. A decision was made to proceed with the XR test market:

> "Recommendation – Proceed with current test market plan. Need to establish a larger case base (need 200 - 300+ cases prior to release) at multiple sites. . . . Test market will provide a degree of confidence in what we expect our complication rate to be . . . . This will help us **determine our associated level of risk and decide what level is too high**." (emphasis supplied)

PowerPoint, G Ex. 38 at 1DOJSYN.089.000087. These determinations, of course, can be made properly only in accordance with FDA regulatory protocol. A test market cannot be used to determine the safety and efficacy of a significant risk device.

Thus, Huggins knew beyond all reasonable question that unauthorized XR clinical studies were planned. He knew about the risks of blood clotting and cement leakage from use of XR in vertebroplasties.

16. Several days later, Josi Hamilton e-mailed Huggins a copy of the minutes of the July 18 meeting. Huggins, demonstrating his complete support of the unauthorized clinical trials of "200 or so" XR cases going forward, responded:

> "We should discuss these minutes . . . I need clarification of a couple of points. We agreed to better document and follow-up on the outcomes of the additional 200 or so cases. We need to understand what the protocol will be to document the cases. Also, we really need to have a conversation with Dr. . . . Chapman who is conducting the studies at Univ. of Wa. . . . ."

Huggins' August 1, 2003 e-mail, G Ex. 41.

17. Huggins, Higgins, and Bohner joined other executives for an August 14, 2003 Strategic Planning Meeting. Minutes, G Ex. 55. Huggins' sole reported contribution to the meeting was that: "Synthes has poor record of PMA approvals . . ." Id. The "Group agreed that focused training [of surgeons] is required" and a decision was made to proceed. Huggins participated in that decision to proceed with the unauthorized clinical trials to experimentally test the "safety of the technique with Norian XR" on human beings. Id.

Thus, in deciding to continue to pursue the 510(k) route, Huggins and the management group explicitly considered Synthes' "poor record of PMA approvals."

18. One month later, on September 19, 2003, a patient of Dr. Paul Nottingham, John Muir Hospital, Walnut Creek, CA died during a spinal surgery using XR. G Exs. 62, 66. No autopsy was done. A medical device report (MDR) was filed, but the report did not mention that the procedure was a vertebroplasty/kyphoplasty using XR.

19. On September 23, 2003, four days after the death of Dr. Nottingham's patient, Huggins met with Josi Hamilton/Synthes Product Manager and co-Defendants Higgins, Bohner, and John J. Walsh. G Exs. 63, 65, 66.

Hamilton, in a September 23, 2003 memorandum prepared for the meeting, G Exs. 62 and 66, summarized her interviews of two of the 19 surgeons selected for the XR clinical trials, stating in part:

> "During cement delivery . . . , a drastic drop in blood pressure was noted. . . . He [Dr. Nottingham] noted a cement leak during injection and feels this was the cause of the incident. He thinks our system is guesswork as to how much material to inject. He thinks a clinical trial is necessary before releasing . . . XR. He said he thought we had much greater clinical experience. **He claimed the sales consultant 'pushed' this product on him and was unclear as to its status on the market.**" (emphasis supplied)

20. Hamilton also interviewed Dr. Joseph Lane on September 26, 2003. Hamilton summarized her interview, stating in part:

> "Lane thinks Norian XR is potentially de-watering and causing episodes of hypotension . . . . With our system he says there is no egress hole so the pressure can be too high . . . with an old fracture, the cement might not have a place to go, so a venous leak can happen . . . . He believes Norian XR should have gone to the IRBs [Institutional Review Boards] of every participating hospital b/c [because] of the information we're collecting. . . . Lane thinks we should go to the FDA ASAP to understand what is necessary in order to change our labeling (Remove 'Not for use in Vertebral Compression Fractures')."

Hamilton's October 1, 2003 e-mail, G Ex. 68.

21. Hamilton, in her October 15, 2003 e-mail to Huggins, Higgins, Bohner, and Walsh, G Ex. 65, informed the recipients of her interviews with all 19 of the surgeons selected to use XR in vertebroplasties to treat vertebral compression fractures and the complications associated with this use of XR on the elderly patient population. She also gave a detailed report about her discussions with the test-market surgeons concerning the death of Dr. Nottingham's patient.

Thus, Huggins was fully advised of the substantial questions raised by Drs. Nottingham and Lane as to the safety of the bone cement. Further, Dr Lane directly asked whether the test market strategy was an appropriate method for the collection of the information Synthes was gathering. He encouraged Synthes to disclose its approach to the Institutional Review Boards of the affected hospitals and the FDA. In short, Dr. Lane urged Synthes to reveal its high-risk approach.

22. Huggins convened a meeting on October 31, 2003, with Higgins, Walsh, and others to consider serious questions concerning the use of XR in the unauthorized clinical trials. Meeting notes, G Ex. 67. Despite the second death and with escalating knowledge of the substantial risks, Huggins and the other participants at the meeting decided to continue the experimental use of XR on humans.

23. On January 22, 2004, a patient of Dr. Hieu Ball, John Muir Medical Center, Walnut Creek, CA died during a kyphoplasty using XR to treat a vertebral compression fracture. An autopsy was done and a medical device report (MDR) was filed. G Exs. 74, 75.

24. Dr. Ball's patient died twelve minutes past midnight on Thursday, January 22, 2004. The surgeon training forum that had been scheduled to begin on Saturday, January 24, 2004, was cancelled. Sentencing Tr. 38:13-19. Additional training fora that had been scheduled through February 2004 were eventually cancelled as well. G Ex. R-23.

25. In the aftermath of the death of Dr. Ball's patient, Huggins signed the February 10, 2004 "Dear Surgeon" letter that was sent to all physicians selected by Synthes to operate in the unauthorized clinical trials. G Ex. 76. The letter did not inform the physicians that the FDA had previously warned against the use of SRS and XR in surgeries to treat vertebral compression fractures. Nothing was stated specifically about the two hypotensive events or the three deaths that had occurred during the use of Synthes' bone cements. No mention was made of the clear warnings by the researchers at the University of Washington that Synthes' bone cements presented potentially lethal risks of leakage and blood clotting. Presented in the guise of a recent epiphany, the letter clearly stated what was long clear to Huggins and the Synthes leadership but which had concealed from the physicians in the test-markets:

> Norian XR, Norian SRS, and Norian CRS are . . . intended for the treatment of bony voids or defects that are not intrinsic to the stability of the bony structure. The use of cements or bone void fillers in the treatment of vertebral compression fractures is intrinsic to the stability of the vertebral body. Accordingly, **Norian XR, Norian SRS, and Norian CRS should not be used in the treatment of vertebral compression fractures.** Additionally, any such use of these products is not consistent with their FDA cleared labeling and is therefore considered "off-label" use. Synthes urges you to seriously consider whether the use of any cement or bone void filler is appropriate in the treatment of vertebral compression fractures." (emphasis in original)

26. The FDA investigated Synthes from May 11 through June 18, 2004. FDA Establishment Inspection Report, G Ex. 79. During the FDA's inspection, Huggins was interviewed by FDA Inspector, Captain Joseph L. Despins, Ph.D. Sentencing Tr. 40:17-63:17, Nov. 21, 2011 (Despins' testimony). In response to Despins' questions, Huggins was unable to recall many facts. He made numerous material misrepresentations of fact about the SRS and XR test markets and his knowledge about the unauthorized clinical trials. Huggins denied knowledge of much that had occurred, even though he had been contemporaneously advised of most events, and those denials professed little to no knowledge of the substance of many meetings, some of which he had chaired:

> "[Despins] asked Mr. Huggins if it was possible that the vertebroplasty test markets for Cavity Creation System and Norian SRS evolved into the subsequent test markets in 2003. Mr. Huggins stated that this would be speculation, and repeated the statement that it would be speculation."
>
> "Mr. Huggins stated he did not know who called the [July 18, 2003 safety] meeting, and that he did not have the knowledge of the meeting exactly, and he did not know who wrote the minutes of meeting."
>
> "Mr. Huggins stated that he believed the outcome [of the safety meeting] was to continue with the University of Washington studies and to make sure the training was appropriate. . . . Regarding the Test Market Plan, he stated that he was not certain if that was what happened or not. . . . [On further questioning and confrontation with documents, Despins] asked Mr. Huggins if an outcome of the meeting on 7/18/2003 [was] to proceed with the Phase 2 Norian XR Test Market, and Mr. Huggins stated yes. I asked him who was the approving official for these outcomes, and Mr. Huggins stated as a group we agreed with the recommendation to go forward. I asked Mr. Huggins if, by being the most senior person at the meeting, if he was the approving official, and he stated that he was."
>
> "[Despins] asked . . . if [Huggins] was aware of this meeting [on September

> 23, following the death of Dr. Nottingham's patient on September 19, 2003] . . . Mr. Huggins stated he did not recall who organized the meeting but it could have been him. He stated the discussion was on the MDR and he was struggling to remember the details."

FDA Establishment Inspection Report, G Ex. 79 at 88, 89-90, 91, 87-93; see also Sentencing Tr. 55:14-20, 59:19-61:25.

27. The FDA's Inspector, Joseph Despins, testified that a lawful test market would allow a medical device manufacturer to gather information from end-users about the device's ease of use for indications that have been cleared by the FDA. Id. at 44:18-45:8. A test market may not be lawfully conducted to test the safety and efficacy of a device. Id. at 55:23-56:11. Despins found that Synthes' test market for XR was conducted to evaluate the safety and efficacy of the product:

> "I was kind of shocked that such activity would be considered in humans in light of the fact that they knew that it could cause problems in the subject - - in an animal."

Id. at 56:2-3, 58:1-7. Despins further testified that before putting XR into the marketplace, Synthes should have followed FDA regulations, which are: "obtain investigational device exemptions [IDEs], present protocol to FDA and a research plan, proposed consent document." Id. at 45:10-46:25. Clinical investigators should have been engaged only after an IDE had been obtained and the research protocol had been submitted to an institutional review board (IRB) of independent, multi-disciplinary professionals. Id. at 47:2-49:2. In a lawful clinical trial:

> "[O]ftentimes it's a back and forth kind of review between the IRB with changes that are recommended to the consent form. It goes back to the clinical investigator and those changes are made. . . . [I]t's resubmitted to the institutional review board and approval is granted by the IRB for typically twelve months . . . . If there's considerable risk to the patient, you could have a six month duration before what's called continuing review by the IRB where the investigator presents a status report, summary of data and any adverse events that may have occurred."

Id. at 48:14-18. Despins found that Synthes did not do obtain an IDE before SRS and XR were experimentally tested on human beings. Id. at 49:6-11, 51:23-53:7.

28. Huggins participated in drafting Synthes' fraudulent and deceptive response to the FDA's investigation. Collectively, Huggins and his fellow executives falsely stated that no clinical trials had occurred, that the test market had been conducted only for cleared indications, that the test market was not conducted for the purpose of testing the safety and efficacy of the bone cements, and that Synthes had not trained the surgeons to use the

cements. See Nov. 5, 2004 Warning Letter, referencing Synthes' July 7 and August 18, 2004 written responses to Form FDA 483, G Ex. 79, FDA Establishment Inspection Report at 130 & 1DOJSYN.021.003331-003337.

29. On November 5, 2004, the FDA issued a warning letter to Synthes, stating in part:

> "During the inspection . . . , the FDA learned that your firm is marketing the Norian XR for new intended uses without approval or clearance from the FDA, in violation of the Act. We also found violations of the Medical Device Reporting regulation . . . ."

G Ex. 79, FDA Establishment Inspection Report at 1DOJSYN.021.003329-003337.

CLAIMS OF ERROR

Pursuant to 18 U.S.C. 3143(b)(1)(B)(iv), Defendant orally moved at the sentencing hearing for release at the expiration of six months of imprisonment, absent a contrary ruling by a court. Sentencing Tr. 83:2-86:3. Defendant's notice of appeal appears to raise the claim that the denial of release was error. We discuss in turn the two reasons presented at the sentencing hearing to support the motion for release. Our explanation also provides further support for our decision to vary upward from the recommended Sentencing Guidelines range.

A. The Court appropriately considered relevant conduct.

Defendant submits that under United States v. Messerlian, 793 F.2d 94 (3d Cir. 1986), it is "fairly debatable" that a preponderance standard of proof should not apply to the sentencing determination. Defendant maintains that a higher standard, at least clear and convincing, if not proof beyond a reasonable doubt, should be applied. Sentencing Tr. 83:16-22; see Messerlian, 793 F.2d at 96 (discussing the meaning of a "substantial issue" that is "fairly debatable" or "close"). Defendant does not present any fairly debatable, substantial issues of law or fact, which if determined favorably to Defendant, would be likely to result in reversal of his conviction, an order for a new trial, or a reduced sentence.

Defendant does not mention or address United States v. Fisher, 502 F.3d 293, 307 (3d Cir. 2007), which is more recent precedent from our Court of Appeals and controls this Court's sentencing determination. Fisher was decided after Rita v. United States, 551 U.S. 338 (2007) and United States v. Booker, 543 U.S. 220 (2005). Fisher instructs that since the Supreme Court's decisions in Booker and Rita, and its own decision in United States v. Grier ("Grier II"), 475 U.S. 556, 568-71 (3d Cir. 2006), "conduct relevant to sentencing enhancements must be proven by a preponderance of the evidence, and the resulting sentence is reviewed for substantive reasonableness on appeal." Fisher, 502 F.3d at 307. As our Court of Appeals has also instructed, "sentencing judges are free to find facts by a preponderance of the evidence, provided that the sentence actually imposed is within the statutory range, and is reasonable." Id. at 305 (citing Grier II, 475 U.S. 556, 568-71 (3d Cir. 2006)).

Defendant also submits that the factual bases for this Court's rulings on relevant conduct, under any standard of proof, do not support the upward variance. Sentencing Tr. 83:23-84:1. We do not agree. "'[A] judge may appropriately conduct an inquiry broad in scope, largely unlimited either as to the kind of information he may consider, or the source from which it may come.'" Fisher, 502 F.3d at 299 (quoting the "fundamental sentencing principle" that was reaffirmed in United States v. Grayson, 438 U.S. 41, 50 (1978)); accord Dawson v. Delaware, 503 U.S. 159, 164 (1992); USSG § 1B1.3; 18 U.S.C. § 3553. The process due an accused at trial differs from the process due a convicted person at sentencing. Fisher, 502 F.3d at 298-99. In reaching a sentence of imprisonment, the Court properly considered Defendant's conduct relevant to the offense of conviction as well as information concerning the safety and efficacy of the devices. See USSG § 6A1.3(b) & Commentary, citing United States v. Watts, 519 U.S. 148, 157 (1997) for the proposition: "Any information may be considered so long as it has sufficient indicia of reliability to support its probable accuracy." Importantly, having carefully reviewed the extensive record and after full consideration of the arguments of the parties, we arrive at our factual findings beyond any reasonable question. The sad truth is that Huggins knew the 510(k) route was inappropriate and unlawful and he, and his corporate conspirators, surreptitiously committed to a course of experimentation on humans in order to capture a large share of a growing, and extremely lucrative, market.

B. The sentence imposed was substantively reasonable.

Huggins maintains that the certainty of his exclusion from the industry by the Department of Health and Human Services, the maximum fine of $100,000 he has agreed to pay, the restrictions already inflicted on his liberty, and other collateral consequences he has suffered as a result of the criminal prosecution, are sufficient punishment to satisfy the goals of sentencing. We disagree. Probation or even a sentence within the Guidelines range of 0 to 6 months would not adequately encompass the societal harm Huggins inflicted.

Any sentence imposed needs to be a fair balancing of considerations. As an initial matter, the Court properly considered and balanced each and every § 3553(a) factor and every argument offered by Defendant for mitigation of sentence. Defendant's individual history, experience, education, professional achievements, impressive good works and charitable acts, and personal and family circumstances were fully taken into account. Sentencing Tr. 5:24-6:24, 7:12-20, 11:17-14:16, 74:13-14. Indeed, this Court accepted most of Huggins' characterizations of his background and character. Huggins' wide reputation as a good man and highly respected professional was commended and taken into account. Id. at 64:5-66:14. Moreover, his reputation in his professional community as "one of the most ethical persons in this whole field" was expressly credited. Id. at 66:14. Indeed, Huggins with credited with having "lived your life, as your friends and your family and your colleagues saw it, in a good way." Id. at 66:3-5. The Court further agreed that there was no need for specific deterrence because there was no worry that Huggins would commit another crime. Id. at 75:11-14. There is no dispute that Huggins poses no risk of flight or immediate danger to the community. Defendant was credited for his guilty plea. Id. at 76:23-77:4, 77:11-18.

Huggins' actual conduct in choosing to pursue the unauthorized clinical trials far overshadows his personal attributes. This case does not involve standard Park-doctrine[6] behavior, in which an unaware corporate official is held strictly liable for the conduct of his subordinates. This matter presents the question of the sentencing consequences of the direct, knowing, intelligent, and intentional choices made by Huggins himself. Huggins, as reflected in his comments at the meetings, knew that conducting clinical trials through the 510(k) route was improper. Nonetheless, in part because Synthes "has [a] poor record of PMA approvals," the 510(k) route was chosen. G Ex. 55. The extreme risks created by the Synthes product – indeed, the uncertain nature of the product itself – was repeatedly brought to the attention of Huggins and his fellow executives by medical consultants, researchers, and surgeons who had used the product only to experience serious complications. These strident and abundant warnings were expressly considered and ignored. Huggins and his confederates closed their eyes to the deaths of two unsuspecting patients who, as it turned out, were little more than subjects in a Synthes experiment. It took a third death before Huggins and his subordinates chose to comply with the unwavering directives of the FDA: XR is "[n]ot intended for treatment of vertebral compression

[6] See United States v. Park, 421 U.S. 658 (1975).

fractures." Persons under Huggins' direction did not even report the first death as required by law, and their report of the second death neglected to mention the critical fact that the surgery was a vertebroplasty using Synthes' product.

In 2002, the FDA refused to authorize the product for use in vertebral compression fractures and at that time, Synthes assured the FDA that it would not promote the product for such indications. We now know, of course, that such was Huggins' and Synthes' hidden, but well-documented, goal. Their circumvention of the FDA's regulatory authority did not end there. When Huggins was interviewed during the May 2004 inspection, he disavowed knowledge of several years of decisions, which had been made at the highest level of corporate governance, and in which he had personally participated. This pattern of deception is unparalleled. As the FDA Inspector, Captain Despins explained, the purpose of a test market is not establish the safety and efficacy of a product, which would be a fundamental error. Sentencing Tr. 56:6-11. Rather, the proper purpose is to "gather information about usability of, in this case, medical devices, how easy it is to handle by the surgeon. . . . [f]or labeled indications, indications that have been cleared by the Food and Drug Administration." Id. at 44:15-45:5; 55:23-56:11 (in contrast, the purpose of the Synthes' test market was "to evaluate the [safety and] efficacy of Norian XR for treatment"). When asked whether in all of his 15 years of experience as an FDA investigator, he had ever seen an analogous situation, Despins testified: "No, sir. This is unique in what I had - - no, I had never seen this before." Id. at 58:24-59:5. Huggins also misled the FDA during the May 2004 inspection and he participated in drafting Synthes' fraudulent and deceptive response to the November 5, 2004 warning letter.

All of the conduct at issue in this matter was carefully planned, studiously assessed, and meticulously implemented by highly-intelligent professionals over a period of years. Huggins personally participated in most of the decisions, and was also the organization's North American leader. All that occurred either happened at his direction, with his full knowledge, or under his command and control. He committed much of the illegal conduct himself. The scope of this behavior and the magnitude of the wrong perpetrated on unsuspecting users of the untested, and unapproved, product was extreme. No similar set of facts can be located in the universe of Park doctrine cases.

The recommended Sentencing Guidelines range of 0-6 months does not adequately address the level of the knowing, intentional, and intelligent choices at issue in this matter. More balanced, and socially aware, leadership was required of Huggins. His failure to provide this leadership resulted in significant harm to the public and deserves stern punishment. Huggins' conduct is not a slight misdeed. For these reasons, we granted an upward variance of three months and ordered immediate surrender.

BY THE COURT:

/s/ Legrome D. Davis

Legrome D. Davis, J.